Medicine®

ABSTRACTS

OPEN

UMIB Summit 2015

UMIB SUMMIT PROCEEDINGS

Editorial – Mariana P. Monteiro

UMIB Summit 2015 was the first international scientific event organized by the Unit for Multidisciplinary Research in Biomedicine. Being a research unit based at a medical school, UMIB's research interests span across a broad field of medical sciences and specialties. Therefore, organizing a multidisciplinary translational research event in an era of increasing specialization, was definitely a big challenge that UMIB decided to undertake. The three host institutions of UMIB, the Instituto de Ciências Biomédicas Abel Salazar of University of Porto, the Santo António Hospital and the Jacinto Magalhães Center of Medical Genetics, both belonging to the Centro Hospitalar do Porto, have gathered their efforts to organize this meeting.

Our aim was not only to present UMIB's latest achievements, but also to bring clinicians and researchers from across different fields in medical sciences together, towards improved advances in the biomedical knowledge and human healthcare. The UMIB Summit has been designed to disseminate UMIB's work by providing an overall view of the active research lines of the unit and of our peer researchers. The event was intended to promote synergies not only within UMIB's research groups, as well as, with other national and international research institutions, some were already ongoing or were emerging collaborations and partnerships. The UMIB Summit was a truly international event focusing on biomedicine, which during the two full days had 270 registered delegates, coming from 14 different countries across Europe, Africa, America and Asia. The program included a plenary lecture on "How to establish successful translational research protocols", by Inmaculada Ibáñez Cáceres from IdiPaz Madrid, which illustrated the example of role model institution dedicated to translational research. There were 7 thematic symposia, organized by the principal investigators of UMIB's research groups, focused on the Immune response to infection, Genetic and neurodegenerative diseases, Mechanisms of cancer treatment resistance, Autoimmune and inflammatory mechanisms, Dysmetabolism and Chronic Kidney Disease, Gastrointestinal Hormones and type 2 Diabetes, and Human Fertility and Reproductive disorders, in which the latest breakthroughs in science were presented. In addition, over 60 oral and 40 posters were presented, distributed by seven different categories, and among these, a panel nominated by the scientific Committee elected the awardees for each category. The past few years have been challenging times for scientific research units and for UMIB in particular, as a result of the well-known nationwide financial constraints. Nevertheless, we strive to continue our consolidation as research unit while remaining adaptable and open to innovative ideas, and the overall success of the UMIB SUMMIT will most certainly contribute to attain these aims.

SYMPOSIA ABSTRACTS

IMMUNITY AND INFLAMMATION

S01 – Immune response in the adipose tissue

Luzia Teixeira, PhD. Unit for Multidisciplinary Research in Biomedicine, Institute of Biomedical Sciences, University of Porto (UMIB, ICBAS-UP) (e-mail: lmteixeira@icbas.up.pt)

The adipose tissue has been increasingly recognized as an organ not only involved in energy homeostasis but also contributing to immune responses. Indeed, inflammation in adipose tissue has been associated with human metabolic disorders. Moreover, it has been shown that the adipose tissue is a reservoir for diverse microorganisms and studies focusing on the immune response to infection in this tissue are arising. In recent years we have been characterizing the immune response elicited in the adipose tissue upon *Neospora caninum* infection, an abortive parasite closely related to *Toxoplasma gondii*. We showed that infection established with a single challenge with this parasite contributes to marked immune cell alterations in the adipose tissue still observed at a chronic phase of infection. Moreover, leptin levels were increased in chronically infected animals suggesting that persistent metabolic alterations may be elicited by infection in the lean host.

Acknowledgements: LT is supported by Fundo Social Europeu and Programa Operacional Potencial Humano through FCT Investigator Grant IF/01241/2014.

S02 – Human Immunodeficiency as a research tool

Ana Espada Sousa, MD, PhD. Instituto de Medicina Molecular, Faculdade de Medicina, Universidade de Lisboa (IMM, FMUL) (e-mail: asousa@medicina.ulisboa.pt)

HIV infection induces a generalized immune activation that is the main determinant of the progressive CD4 T cell depletion that ultimately leads to AIDS in the absence of antiretroviral treatment. HIV-2, like HIV-1, establishes a disseminated infection with persistent viral reservoirs and immune activation. Nevertheless, the plasma viral load is usually undetectable and the CD4 decline rate is very slow in HIV-2-infected individuals. We have been exploring the distinct equilibria established between the host and HIV-1 and HIV-2, not only to better understand HIV immunopathogenesis per se, but also to identify the host's immune system mechanisms to counteract CD4 depletion and limit immunopathology. Moreover, within the scope of our primary immunodeficiency centre, we have been able to combine the provision of differentiated diagnosis and follow-up with the generation of unique knowledge through the study of these naturally-occurring human gene knock-out settings.

S03 – Dendritic cells: central players in orchestration of type 2 inflammation

Andrew S. Macdonald, PhD. Manchester Collaborative Centre for Inflammation Research, United Kingdom (e-mail: andrew.macdonald@manchester.ac.uk)

Dendritic cells (DCs) are specialised innate immune cells that play a key role in initiation and direction of adaptive immunity against diverse immune challenges. However, relatively little is known about precisely how DCs become activated and function in Type 2 settings, either during parasitic helminth infection or following exposure to allergens. We have shown that DCs responding to helminths display an unusual, low level, activation phenotype. Irrespective of this, we have demonstrated that DCs are both sufficient and necessary for induction of Type 2 immunity against several helminth species. Although DCs are clearly centrally involved in coordination of the immune response during Type 2 inflammation, the specific DC subsets that are required, and the mechanism(s) by which they direct Th2 polarisation, remain poorly understood. Our recent work addressing these fundamental issues will be presented.

GENETIC AND NEURODEGENERATIVE DISORDERS

S04 – Alzheimer's disease biomarkers in mouse models of cerebral β-amyloidosis: bridging the translational gap

Luís F. Maia, MD, PhD. Hospital de Santo António, Centro Hospitalar do Porto (HSA-CHP), Portugal (e-mail: luis.lf.maia@gmail.com)

p = 0.001). Diabetic patients were significantly associated with higher 30-day rate of readmission (OR 3.45, p = 0.03), higher rate of rehospitalization at three-months (7.44 vs 22.55 admissions per 100 patient-month, p = 0.003), at six-months (5.27 vs 16.44 admissions per 100 patient-month, p < 0.001) and at one-year (4.65 vs 10.57 admissions per 100 patient-month, p = 0.001). When adjusting for the main cause of admission, DM maintains a trend for significance in association with readmission (OR 3.18, p = 0.057). DM is an important predictor for 30-day readmission and rehospitalization until one year.

CO32 – Pregnancy in renal transplant recipients: obstetric outcomes and risk of allosensitization

Sofia Santos, MD[1], Jorge Malheiro, MD[1,2], Andreia Campos, MD[1], Sofia Pedroso, MD[1], Manuela Almeida, MD[1], La Salete Martins, PhD[1,2], Leonídio Dias, MD[1], Castro Henriques, MD[1], António Cabrita, MD[1]. [1]Nephrology Department, Centro Hospitalar do Porto - Hospital Santo António, Porto, Portugal, [2]Unit for Multidisciplinary Research in Biomedicine – ICBAS, Porto, Portugal (e-mail: sofia.fersantos@gmail.com)

Kidney transplantation improves women's chances of becoming pregnant and of having a live birth. Donor specific anti-HLA antibodies are responsible for antibody-mediated rejection and reduced kidney allograft survival. After pregnancy, woman may develop anti-HLA antibodies after having encountered HLA alloantigens of the fetus inherited from the father. The aim was to describe the outcomes of pregnancies and analyze its impact on *de novo* allosensitization. A retrospective study of all pregnancies occurring in our center since 2010 to 2014, in women with a functioning graft was made; miscarriages during the first trimester were excluded. We assessed maternal and fetal complications: late miscarriage (2nd and 3th trimesters), preeclampsia, fetal malformations, preterm birth, and low birth weight (<2.5Kg). Anti-HLA antibodies were screened before and after pregnancy (solid-phase assay). After pregnancy we examined the evolution and episodes of acute rejection. Within that period, 11 pregnancies occurred in 10 women. We excluded 3 because of missing data. Overall, the live birth rate was 88% (7/8 pregnancies). One pregnancy was interrupted during second trimester because of severe fetal malformation (heart). Preeclampsia occurred in 2 patients and a threat of premature delivery occurred in one case. 3 newborns were premature (<37 weeks) and 2 had low birth weight (<2.5Kg). Delivery was done by caesarean in 6 of the 7 live births. In all cases GFR remained relatively stable during and after delivery. Before pregnancy, no anti-HLA antibodies were detected in any women. After pregnancy, *de novo* allosensitization was detected in 2 of them: they developed *de novo* anti-HLA antibodies, at 9 and 20 months post-delivery. In the 2nd patient, the development of *de novo* anti-HLA antibodies did not have impact on the graft. In the 1st patient, the biopsy performed showed acute antibody-mediated rejection and also acute T-cell-mediated rejection with mild to moderate intimal arteritis (Banff IIA). In spite of the treatment she progressed with renal function decline, having lost her graft function and entering dialysis after 11 months post-delivery. In conclusion, despite complications, the outcomes for pregnancy and kidney allografts are good. In our cohort 1(/8) case of *de novo* allosensitization after pregnancy leading to antibody mediated rejection and consequent graft loss was observed. Careful screening of anti-HLA antibodies emergence after pregnancy in kidney transplant patients is advisable.

CO33 – Risk Factors for Mortality in End-Stage Kidney Disease Patients Under Online-Hemodiafiltration: Three-Year Follow-Up Study

Pedro Sousa-Martins, MD[1], Alexandra Moura, PhD[2], José Madureira, MD[3], Pablo Alija, MD[3], José Gerardo Oliveira, MD[4], Martin Lopez, MD[5], Madalena Filgueiras, RN[6], Leonilde Amado, RN[7], Maria Sameiro-Faria, MD[7], Vasco Miranda, MD[7], Edgar Mesquita, MSc[8], Laetitia Teixeira, PhD[1], Alice Santos-Silva, PhD[9,10], Luísa Lobato, MD, PhD[11,12], Elísio Costa, PhD[9,10]. [1]Instituto de Ciências Biomédicas Abel Salazar, Universidade do Porto, [2]Instituto de Ciências da Saúde, Universidade Católica Portuguesa, Porto, Portugal, [3]Clínica de Hemodiálise NefroServe, Barcelos, Portugal, [4]Centro Hospitalar do Porto, Porto, Portugal, [5]Clínica de Hemodiálise de Felgueira, Felgueiras, Portugal, [6]Clínica de Hemodiálise de Gondomar, Gondomar, Portugal, [7]Clínica de Hemodiálise NephroCare, Maia, Portugal, [8]Núcleo de Estudantes de Estatística, Universidade do Minho, Braga, Portugal, [9]Laboratório de Bioquímica, Departamento de Ciências Biológicas, Faculdade de Farmácia, Universidade do Porto, Portugal, [10]UCIBIO, REQUIMTE, Universidade do Porto, Portugal, [11]Instituto de Ciências Biomédicas Abel Salazar, Universidade do Porto,[12]Serviço de Nefrologia & Departamento de Ensino, Formação e Investigação, Centro Hospitalar do Porto, Portugal (e-mail: emcosta@ff.up.pt)

End-stage kidney disease (ESRD) patients under dialysis have high mortality rate. Inflammation, poor nutritional status and disturbances in erythropoiesis and iron metabolism have been reported in these patients. Moreover, there is a growing concern about the health related quality of life (HRQOL) in the context of ESRD. The aim of this work was to study the predictive value of these disturbances, dialysis adequacy and of HRQOL for mortality risk, by performing a three-year follow-up study. Clinical, socio-demographical and analytical data (dialysis adequacy, nutritional status, hematological data, lipid profile, iron metabolism and inflammatory markers) were obtained from 236 patients (61.02% male; 67.50 [56.00-75.00] years old) under online-hemodiafiltration. Patient's reported HRQOL score was assessed by using the Kidney Disease Quality of Life-Short Form (KDQOL-SF). 54 patients died during the 3 years follow-up period. Our data showed that mean cell hemoglobin concentration (MCHC), transferrin and albumin are significant predictors of mortality. The risk of death was higher in patients presenting lower levels of MCHC (Hazard ratio [HR] = 0.70; 95% confidence interval [CI] = 0.500-0.984), transferrin (HR = 0.99; 95% CI = 0.982 – 0.998), and albumin (HR = 0.96; 95% CI = 0.938-0.994). Our study showed that poor nutritional status and an inflammatory-induced iron depleted erythropoiesis are important factors for mortality in these patients. MCHC, transferrin and albumin may provide useful biomarkers of risk in ESRD patients under OL-HDF.

CO34 – Impact of de novo donor-specific anti-hla antibodies in kidney graft failure: a case-control analysis

Jorge Malheiro, MD[1,3], Sandra Tafulo, MD[2,3], Leonidio Dias, MD[1], La Salete Martins, MD, PhD[1,3], Idalina Beirão, MD, PhD[1,3], António Castro-Henriques, MD[1,3]. [1]Nephrology & Kidney Transplantation Unit – Hospital de Santo António, Centro Hospotalar do Porto (HAS-CHP), [2]CSTP - IPST, [3]Unit for Multidisciplinary Research in Biomedicine (UID/Multi/00215/2013) UMIB – ICBAS (e-mail: jjorgemalheiro@gmail.com)

Data on the prevalence and impact of *de novo* donor-specific anti-HLA antibodies (dnDSA) in the process leading to kidney graft (KG) failure are still scarce. We investigated 56 patients transplanted between 2000-2010 with KG failure (cases) and 56 patients with a functioning graft (controls) matched for: donor type, transplant number and year, recipient age/gender, donor age/gender, HLA mismatches and dialysis vintage. All patients had at least one serum collected 1 year before failure or end of follow-up (Dec2014), in which dnDSA detection was performed. Data on the KG pathology was collected considering the last available sample. Mean KG survival years were 9.6 and 4.7 for controls and cases respectively. dnDSA was present in 54% of cases versus 16% of controls (P < 0.001). dnDSA against class I, II and I+II was detected in 27%, 13% and 14% of cases, and 5%, 9% and 2% of controls, respectively (P < 0.001). Delayed graft function was more common in cases (48%) than in controls (21%) (P = 0.003), as was acute rejection (21% in cases, 9% in controls; P = 0.065). At 6-years, 75.5%, 27.8%, 53.8% and 37.5% of grafts survived in patients with no DSA, dnDSA I only, dnDSA II only and dnDSA I+II, respectively (P < 0.001). Cox regression showed that delayed graft function (HR 1.927, P = 0.019) and dnDSA (HR 2.656, P = 0.001) were independent predictors of graft failure, adjusted for confounding factors (acute rejection and type of induction). Forty-two cases and 11 of controls had at least one indication biopsy. Transplant glomerulopathy was present in 18 cases and 4 controls (P = 0.001). Acute antibody mediated rejection was present in 8 cases and 1 control (P = 0.032). Considering only 36 biopsies performed at the same time of dnDSA detection, 22 were done in dnDSA+ patients and 14 in DSA- patients. Transplant glomerulopathy was present in 14 DSA+ and 3 DSA- patients (P = 0.013). Acute antibody mediated rejection was present in 5 DSA+. Graft function in controls at last visit was significantly